

FIG. 1A-1

```

10      20      30      40      50      60      70
GGAGGTATAGGAGCTCTCTTCGATTTTAGCAAAACCAGGAGTCCGAAGATCTAAGGAGAGCTGGGGTTTGACTCC
      SacI      BglII
85      95      105      115      125      135      145
GAGAGCTCGAGCAGTCCCAAGACCTGGTCTTGACTCACGAGTTAGACTCCACTCAGAGGCTGACTGTCTCCAGG
      SacI      PflMI
160      170      180      190      200      210      220
      XhoI      Tth111I
GTCTACACCTCTAAGGGCGACACTGGGCTCAAGCAGACTGCCGTTTCTATATATGGGATGAGCCTTTCACAGGGCAG
235      245      255      265      275      285      295
CCAGTTGGGATGGGTTGAGGTTTGGCTGTAGACATCAGAAACCCAAAGTCAAAATGCGCTTCAACCCAGTAGAAAATT
310      320      330      340      350      360      370
CACCAGCCCGCAGAGCTAAAGTTGGGTGGACATTAGGGTTGTTGATCCAGGAGCTCAACAGTGTCTCTGAGGCC
      SacI
385      395      405      415      425      435      445
CCAGCTCCTTCTGCCCCCACCACCATCTTCAGTGCTGCTTCTCTCAAGGCCACAGCTGTAGTTGGCCAGGGG
      PvuII      BglI
460      470      480      490      500      510      520
GCTTCATTAATTTTGTCTCTGGCAGTAGGAGGAAGAGATGAATGCTCTCCATGGGTCTTTCTTAGGAATGT
      NcoI
535      545      555      565      575      585      595
GGGAACCTTTTCCAGAAAGTCTCTATGTCTTTTAGTTTGTGTTGGGTCACTTGCCCTTCCCTGAACCACTTCTCTGAC
610      620      630      640      650      660      670
TCCTGGACAGGATGTGCACTGATGAGCTTAGCTTTGGGGATCTAATAGTGACTTTACAAAGCCTCTTTTGAGAAGG
      ApaLI      EspI
685      695      705      715      725      735      745
TGACATTGGAACCAAGGCTTGAGCAGACACAAACAAAGATTGCAGGGAGGGGCATTGCAGGTGGAGGAACGGCAC
      BspMI
760      770      780      790      800      810      820
ATGCAAGAGCCCTGCGTGGGAGTGAGCTTGGTGGTTTGGTCAATCAGTTGTCTCAGAGCACACCGGGCCCTGTCTAGCTA
      ApaI
      EcoO

```

FIG. 1A-2

```
835 855 865 875 885 895
GGCACAGCCTGGGCGCTGCTCTGAGTATGACAGAGAGCCCTGGGAAGTTGTAGGTGGAGGAAAGACAGGTCATGA
910 920 930 940 950 960 970
CTAGGAAAAAGCAATCCCTCTGTTGTGGGTGGAGGAAGTTGCAGTGTGTGTGAGAGAGAGACAAGACAGAC
985 995 1005 1015 1025 1035 1045
AGACAGACACTTCTCAATGTTTACAAGTGCTCAGGCCCTGACCCGAATGCTTCCAAATTTACGTTCTGGAAA
1060 1070 1080 1090 1100 1110 1120
ACCCCTGTATCATTTTCACTACTCAAAAGAAACCTCGGGAGTGTCTTCTCTGAAAGGTCAACAGGTTTGTGACTC
1135 1145 1155 1165 1175 1185 1195
TCTGCTGTCTCATTTCTTCTTGTGCTGGTGGTGATGGTTGCTTGTCCAGGCCCTGTCCCGCATCCTCTTGGCCC
1210 1220 1230 1240 1250 1260 1270
CTGCAGAGGGATGAGTGTGTGGGGCCTCACGAGTTGAGTTGTTTCATAAGCAGATCTCTTTGAGCAGGGCGCCT
PstI BglII NarI Ps
1285 1295 1305 1315 1325 1335 1345
GCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGGAATCCAGGCAGATGTAGCATTTAAACAACA
tI DraI
1360 1370 1380 1390 1400 1410 1420
CACGTGTATAAAAGAACCAAGTGTCCGCAGAAAGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAA
1435 1445 1455 1465 1475 1485 1495
TGGGCATTGGCACCTCCCTTAGTAGGGCCTTTGCTGGGGGTAGAAATGAGTTTAAAGGCAGGTTAGACCCCTCGA
1510 1520 1530 1540 1550 1560 1570
ACTGGCTTTTGAATCGGGAATTTACCCCCCAGCCGTTCTGTGCTTCATTGCTTCACTACATCACTGCCCTAAGATG
1585 1595 1605 1615 1625 1635 1645
GAGGAACCTTTTGATGTGTGTGTCTTCTCTCCTCACTGGGCTCTGCTTCTTCACTTCCCTTGTCAATGCAGAGAA
1660 1670 1680 1690 1700 1710 1720
CAGCAGCAGGCACCCAGAGGCAGGCCCTTGTAAAGAACGACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGG
StuI BspMI
1735 1745 1755 1765 1775 1785 1795
TAAGGGGCTGGCTGGGTCTGTCTTGGGTGTGGGCCCTCTGGCGTGGGCTCCACAGGCAGCGGGTGTGTGTCTCA
ApaI EcoO
```

FIG. 1A-3

Inventor(s): Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

FIG. 1A-4

2710 2720 2730 2740 2750 2760 2770
 ATTGCCATGTCATGACTTTTGGGGGCCCTTGGCCGTTAAATAAAATCAAAATTGTACTTTATGACTGGTTT
 ApaI
 EcoO
 2785 2795 2805 2815 2825 2835 2845
 GGTATAAGAGGAGTATAATCTTCGACCCTGGAGTTTCATTTATTTCTCCTAATTTTAAAGTAACTAAAGTTGT
 DraI
 2860 2870 2880 2890 2900 2910 2920
 ATGGGCTCCTTTGAGGATGCTTGTAGTATTGTGGTGCTGTTACGGTGCCTAAGAGCACTGGGCCCTGCTTCA
 ApaI
 2935 2945 2955 2965 2975 2985 2995
 TTTTCCAGTAGAGGAAACAGGTAAACAGATGAGAAATTTTCAGTGGGGCACAGTGATCAGAAGCGGGCCAGAG
 3010 3020 3030 3040 3050 3060 3070
 GATAATGGGATGGAGAGATGATGGGGACCCATGGGCCATTTCAGTTAAATTTTCAGTCGGGTCCACCAGGAAGAT
 EcoO NcoI
 3085 3095 3105 3115 3125 3135 3145
 TCCATGTGATAATGAGATTAAACGTGCCAGTCACGGCGACACTCAGTAGGTGTTATTCCTGTCTGCGCAACAGCA
 3160 3170 3180 3190 3200 3210 3220
 ACCATAGTTGATAAGAGCTGTTAGGGAATTTGTCTTTTGTCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTA
 EcoO
 3235 3245 3255 3265 3275 3285 3295
 GCTCCCTGTCAATGACATCATCTGAGCCTTTCTGCTACTGATCATCCACCCTGCCCTTGAATGCTTCTAGTGAC
 BsmI+
 3310 3320 3330 3340 3350 3360 3370
 AGAGAGCTCACTACCAGGACTACTCCCTCTTTCATTTAGTAATCTGCCCTCCTTCTTTTCTGTCCCTGTCTGT
 SacI
 3385 3395 3405 3415 3425 3435 3445
 GTGTTAAGTCCCTGGAGAAAAATCTCATCTATCCCTTTTCATTTGATTCTGTCTTTTGAGGGCAGGGGTTTGT
 3460 3470 3480 3490 3500 3510 3520
 CTTTGTGTTGTTTTTAAAGTGTGTTTCCAAAGCCCTTGCTCCCTCCTCAATTGAAACTTCAAAGCCCTCAT
 3535 3545 3555 3565 3575 3585 3595
 TGGGATTGAAGGTCCTTAGGCTGGAAACAGAGAGTCTCCCAACCTGTTCCCTGGCCCTGGATGTGTGTGTG
 EcoOMstII

FIG. 1A-5

3610 3620 3630 3640 3650 3660 3670
TGCAGTATCCCTGGAAGGTGCCAGGCATGTCTCCCGGCTGCCAGGGACACATCTCTATCCTTCTCCAACCC
3685 3695 3705 3715 3725 3735 3745
CTGCCCTTCATGGCCCATGGAACACAGGAGTGCCCATGCCCTGTGTGCACCTACTTCCATCAGTATTTCAACAGAGAT
BgII NcoI
3760 3770 3780 3790 3800 3810 3820
CTGCAGGATCAAAAGTGAATTTCTCCAGGGATTGTGAAATGATGCGATTGTGGTCATGTTTAAAGGGGGCAACTGT
I EcoRI
PstI
3835 3845 3855 3865 3875 3885 3895
CTTCTAGAGAGTCTGATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTTAAATCATTTCAAG
XbaI
3910 3920 3930 3940 3950 3960 3970
GTGGAGCAGGTGGGAAGGTATGGATGTGTAAAGATTGAAATTTGTCCATCATAAATGTGTAAAGCATGCT
BspMI-
3985 3995 4005 4015 4025 4035 4045
GGCCTATGTCAGCAGTCACAGCCTGGAGGTGGTAACAGAGTGCCAGTCACTGATGCTCAAGCCTGGCACCTACAG
4060 4070 4080 4090 4100 4110 4120
TTGCTGGAACCCAGAAAGTTTCACGTTGAAACAAACAGGACAGTGGAATCTCTGGCCCTGTCTTTGAACACAGTGGC
4135 4145 4155 4165 4175 4185 4195
AGATCTGCTAACACTGATCTTGGTTGGCTGCCGTACGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTTGGCTTAGT
BgII
4210 4220 4230 4240 4250 4260 4270
CCCCGCTATTCCTTATTTGCTTACCTCGGTCTATTTTGTCTTATCAGTGGACCTCACGAGGCATCATAGGCATTT
4285 4295 4305 4315 4325 4335 4345
GAGTCTATGTGTCCCTGTCCACATCCTCTGTAAAGGTGCAGAGAAAGTCCATGAGCAAGATGGAGCAGTCTTAGTG
4360 4370 4380 4390 4400 4410 4420
GGTCCAAAGTCAGGACACTATTCAGCAATCTACAGTGCACAGGGCAGTTCCCAACAGAGAATTACCTGGTCTG
ApaI
4435 4445 4455 4465 4475 4485 4495
AATGTCGGATCTGGCCCCCTTCCCTTCCCACTGTATAATGTGAAAACCTCTATGCTTTGTTCCCTTGTCTGCAAA
4510 4520 4530 4540 4550 4560 4570
ACAGGGATAATCCCAAGAACTGAGTTGTCCATGTAAAGTCTTAGAACAGGGAGTGCTTGGCTTGGGAGTGTAC
Bs

FIG. 1A-6

4585 4595 4605 4615 4625 4635 4645
CTGCAGTCAATTCATTATGCCCCAGACAGGATGTTTCTTTATAGAAACGTGGAGGCCAGTTAGAACGACTCACCGCT
pMI+
PstI
4660 4670 4680 4690 4700 4710 4720
TCTCACCACTGCCCATGTTTGGTGTGTGTTTCAGGTCCACTTCATCAACCCGGAAACGGTGCCCCAAGCCCTGCT
PflMI
4735 4745 4755 4765 4775 4785 4795
GTGCGCCACGCGAGCTCAATGCCATCTCCGTCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA
4810 4820 4830 4840
GAAACATGGTGTCCGGCCCTGTGGCTGCCACTAGCTCCTCCGA

FIG. 1B

CONSENSUS PROBE 20 30 40 50 60 70
 GATCCTAATGGGCTGTACGTGGACTTCCAGCGGACGCTGGGCTGGGACGACTGGATCATCGCCCCCGTCG
 ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** **
 TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
 OP4 28 38 48 58 68 78 88

 80 90 100 110 120 130 140
 ACTTCGACGCCCTACTACTGCTCCGGAGCCTGCCAGTTCCCTCTGCGGATCACTTCAACAGCACCAACCA
 ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** **
 GCTACGCGCGCTACTACTGTGAGGGGAGTGTGCCCTTCCCTCTGAACCTCTACATGAACGCCCAACCA
 98 108 118 128 138 148 158

 150 160 170 180 190 200 210
 CGCCGTGTGCAGACCCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAGCCCTGCTGCGTGCCCAAC
 *** ** ** ** **
 CGCCATCGTGACAGCGCTGGTCCACTTCAATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCACG
 168 178 188 198 208 218 228

 220 230 240 250 260 270 280
 GAGCTGTCCGCCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGAAGAACTACCAGGAGA
 *** ** ** ** *
 CAGCTCAATGCCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA
 238 248 258 268 278 288 298

 290 300 310
 TGACCGTGTGGGCTGCGGCTGCCGCTAACTGCA
 ** ** ** *
 TGGTGTCCGGGCTGTGGCTGCCACTAGCTCCT
 308 318 328

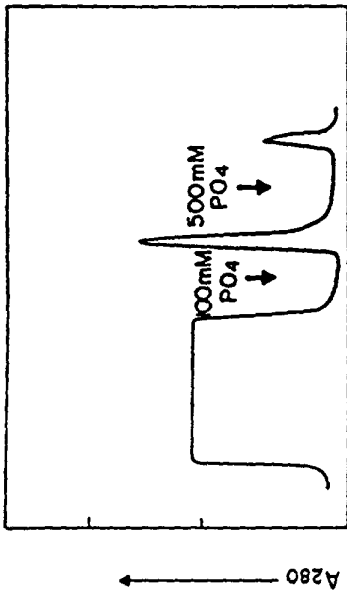


FIG. 2B

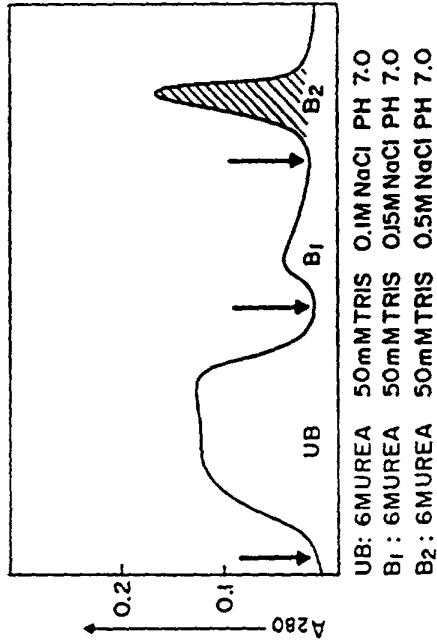


FIG. 2D

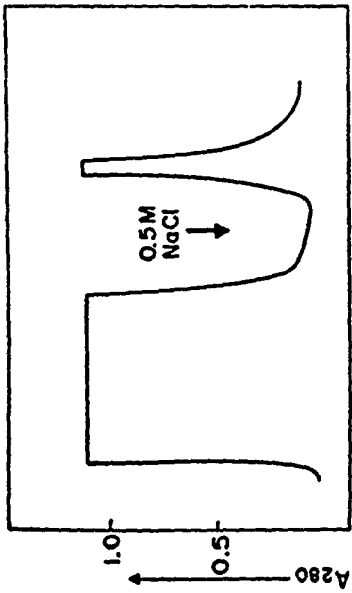


FIG. 2A

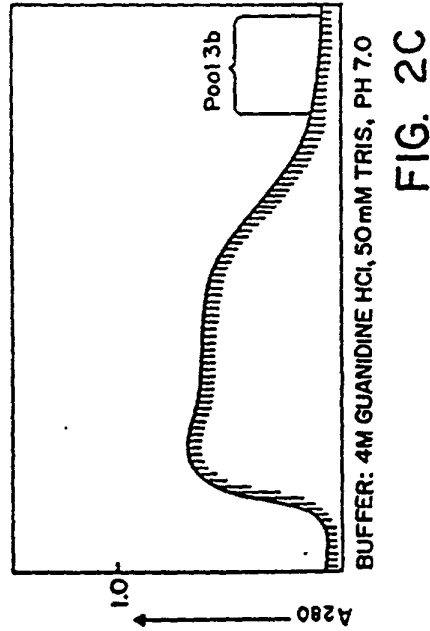


FIG. 2C

FIG. 3A FIG. 3B

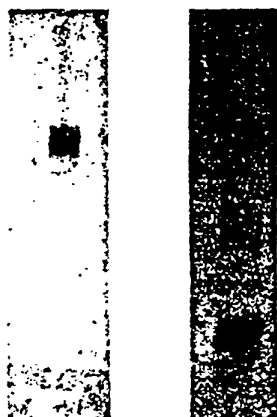


FIG. 4A FIG. 4B



FIG. 5



*



1

2

FIG. 6 A FIG. 6 B FIG. 6 C FIG. 6 D FIG. 6 E

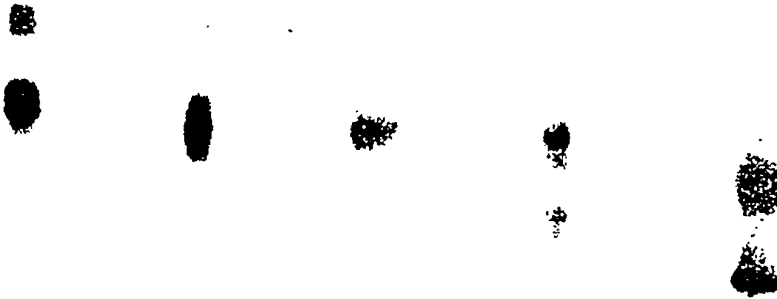
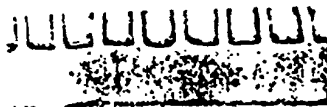


FIG. 15



— NON-REDUCIBLE 30K

— 18K SUBUNIT
— 16K SUBUNIT

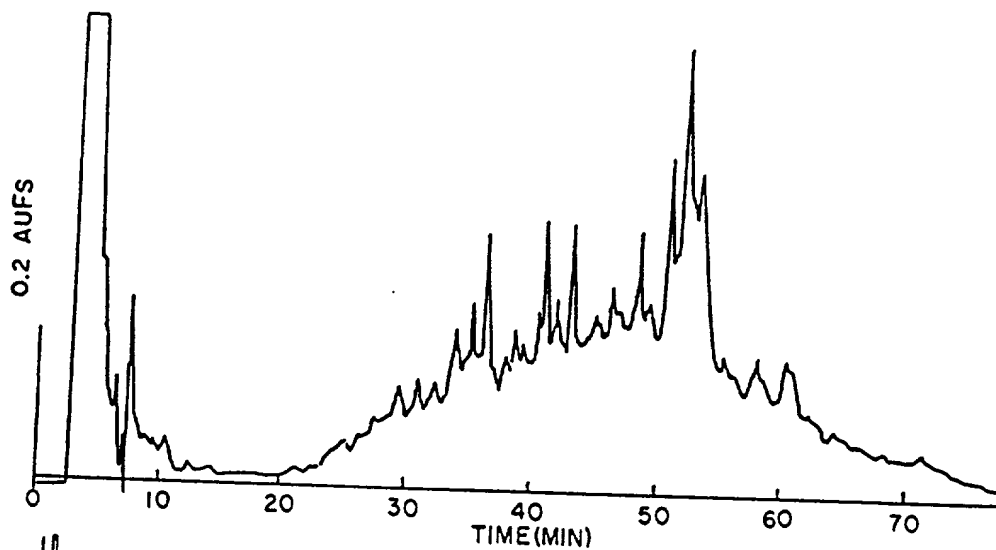


FIG. 7A

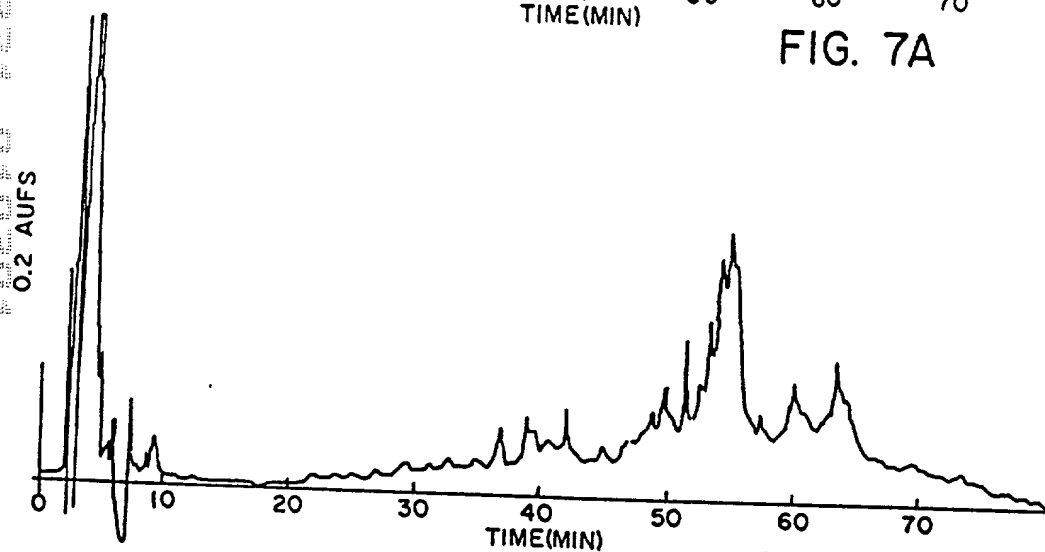


FIG. 7B

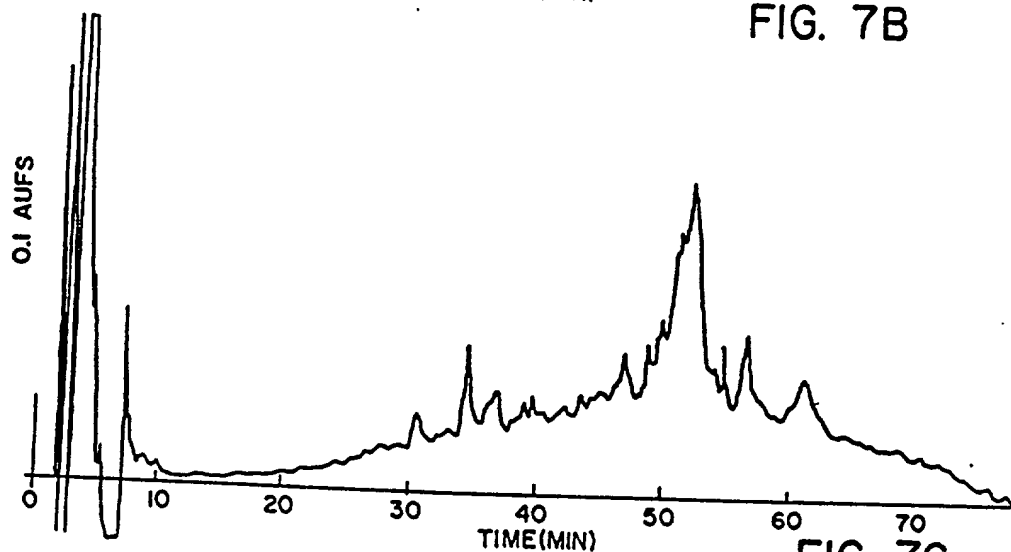


FIG. 7C

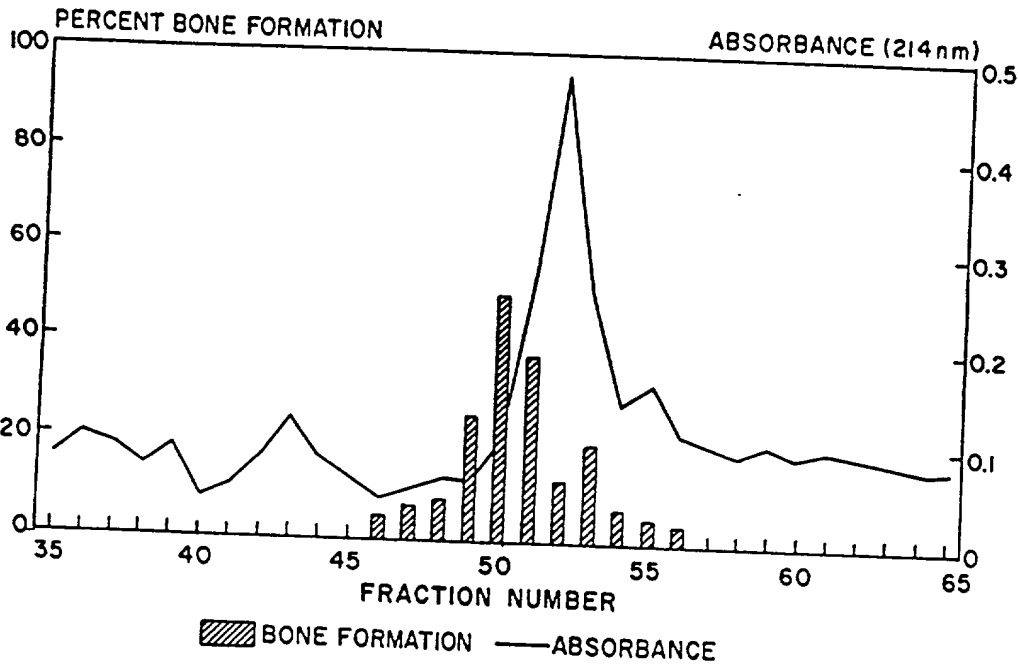


FIG. 8

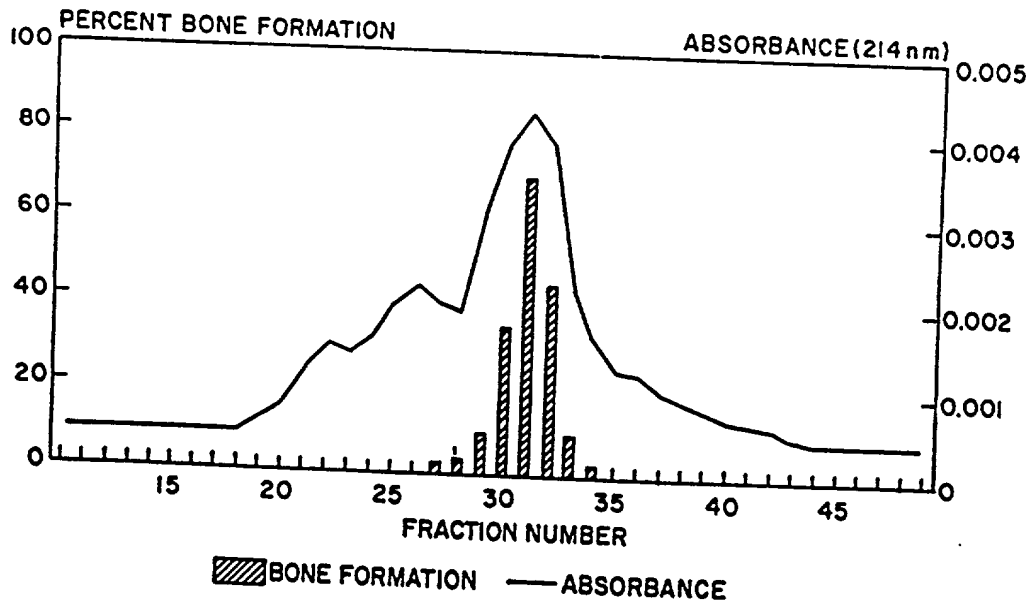


FIG. 9

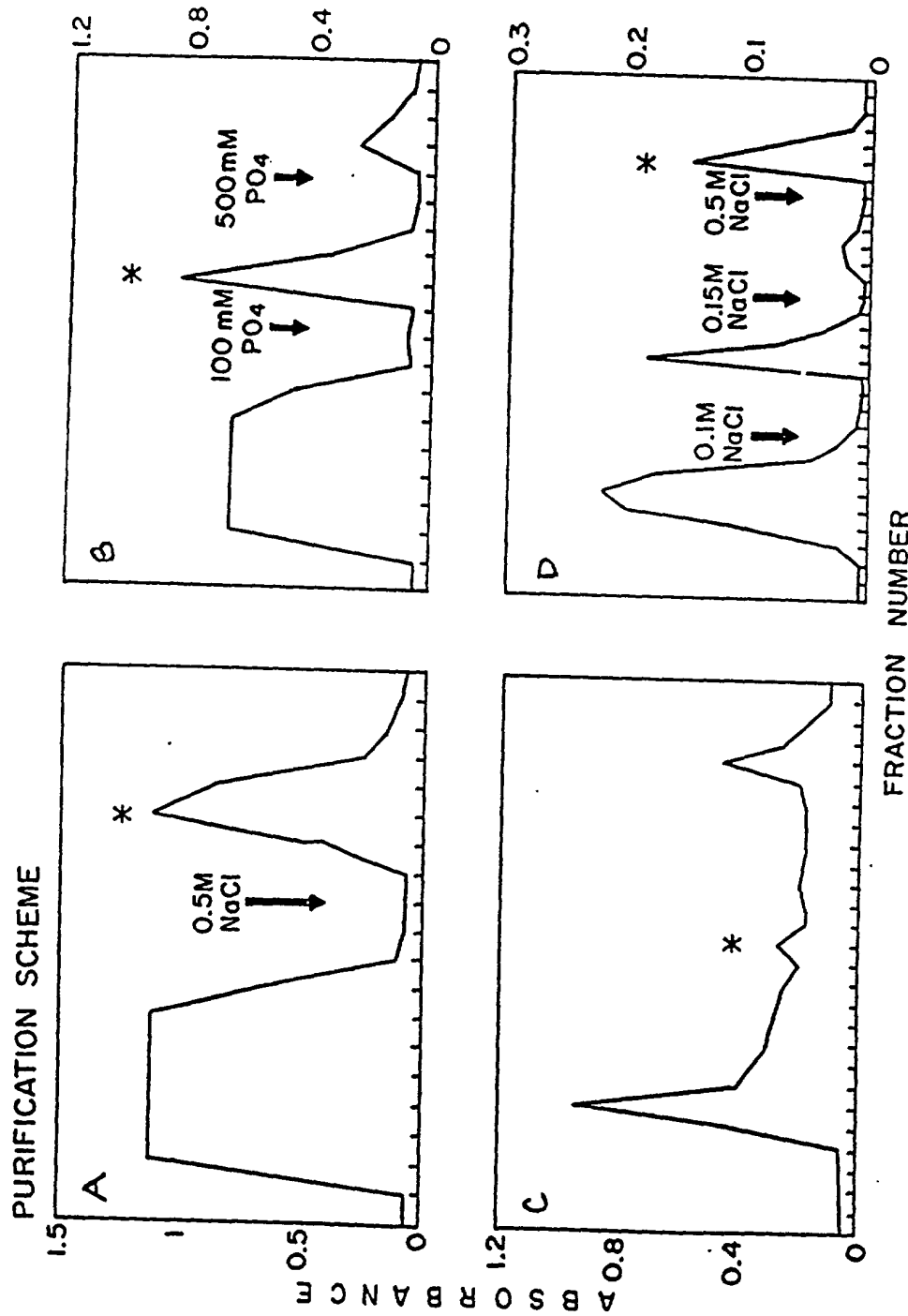


FIG. 10

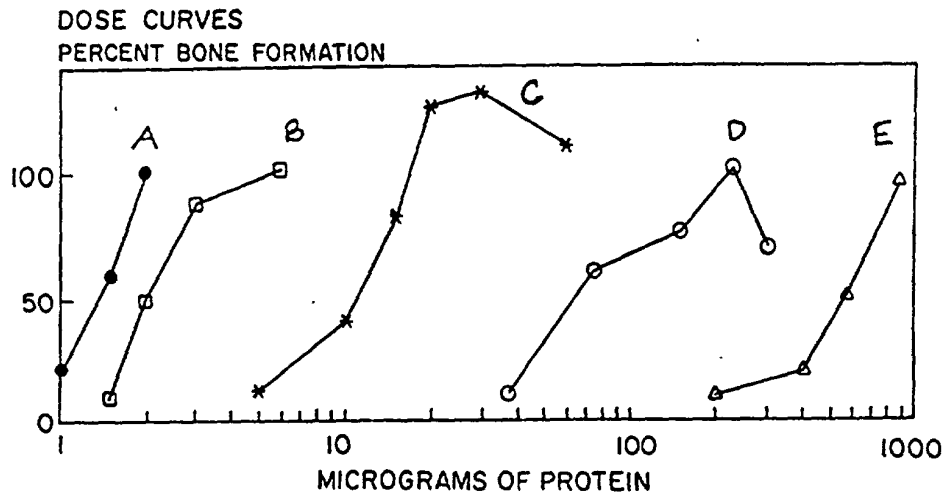


FIG. 11

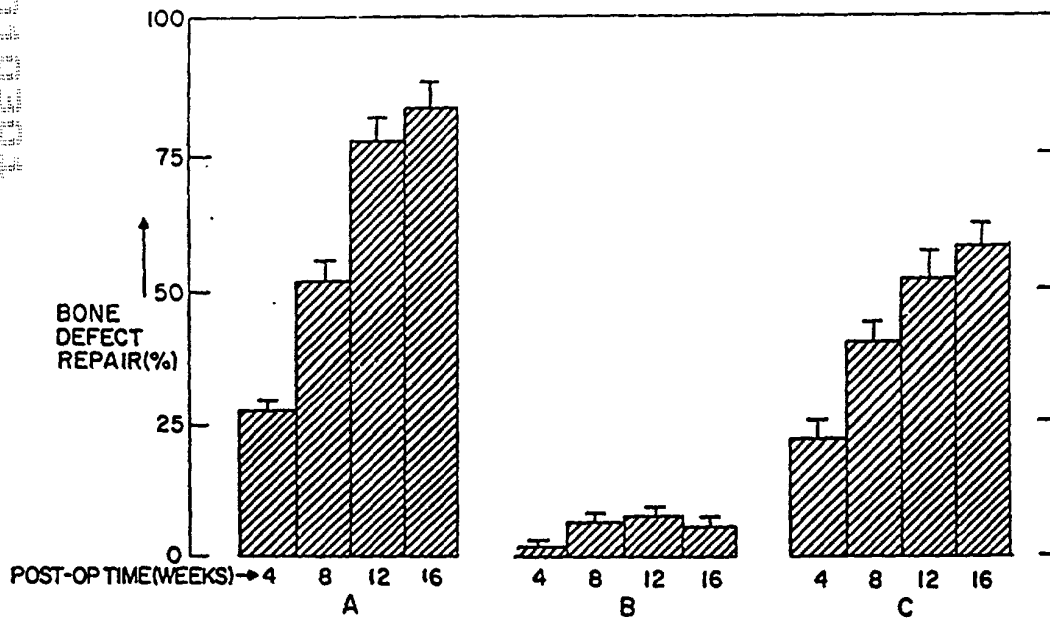


FIG. 12

FIG. 13

10 20 30 40 50
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGA
D P N G L Y V D F Q R D V G W D D

60 70 80 90 100
CTGGATCATCGCCCCCGTCGACTTCGACGCCTACTACTGCTCCGGAGCCT
W I I A P V D F D A Y Y C S G A

110 120 130 140 150
GCCAGTTCCCTCTGCGGATCACTTCAACAGCACCAACCACGCCGTGGTG
C Q F P S A D H F N S T N H A V V

160 170 180 190 200
CAGACCCTGGTGAACAACATGAACCCCGCAAGGTACCCAAGCCCTGCTG
Q T L V N N M N P G K V P K P C C

210 220 230 240 250
CGTGCCCAACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATT
V P T E L S A I S M L Y L D E N

260 270 280 290 300
CCACCGTGGTGCTGAAGAACTACCAGGAGATGACCGTGGTGGGCTGCGGC
S T V V L K N Y Q E M T V V G C G

310
TGCCGCTAACTGCAG
C R *

SDS GEL ELUTION OF OSTEOGENIC ACTIVITY
 CALCIUM CONTENT (ug/mg tissue)

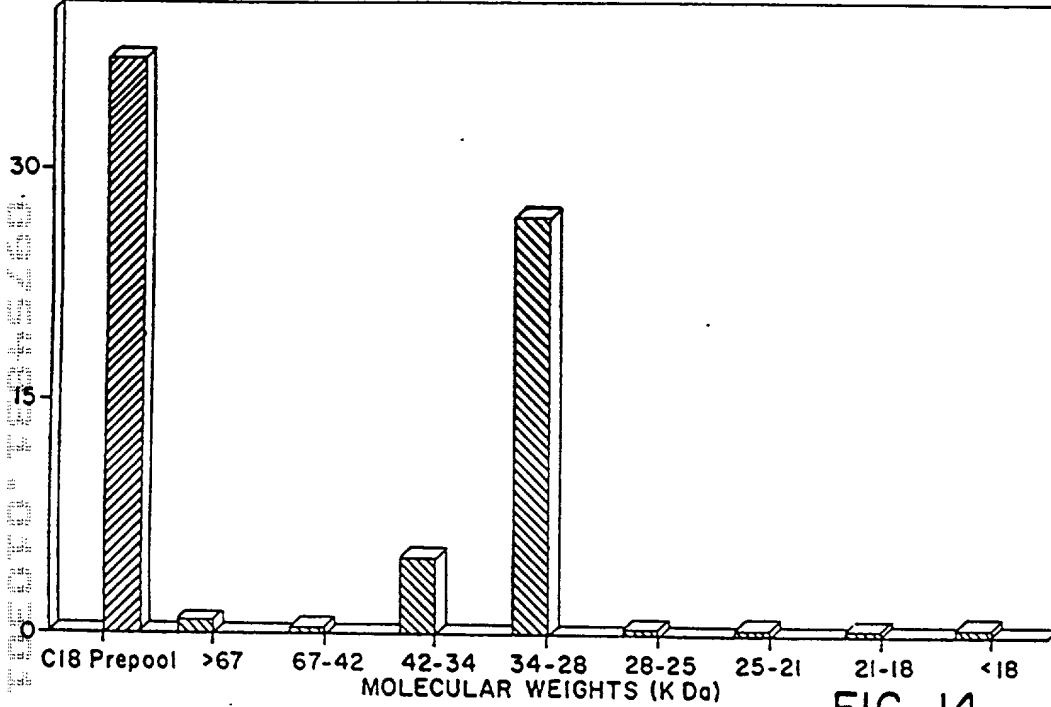


FIG. 14

ALKALINE PHOSPHATASE (U/mg protein)

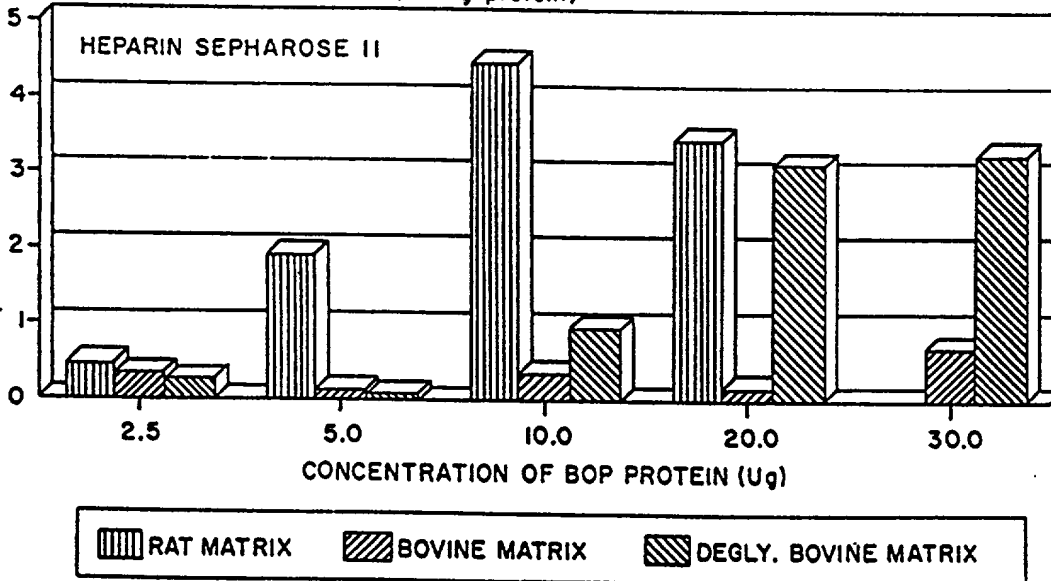


FIG. 19

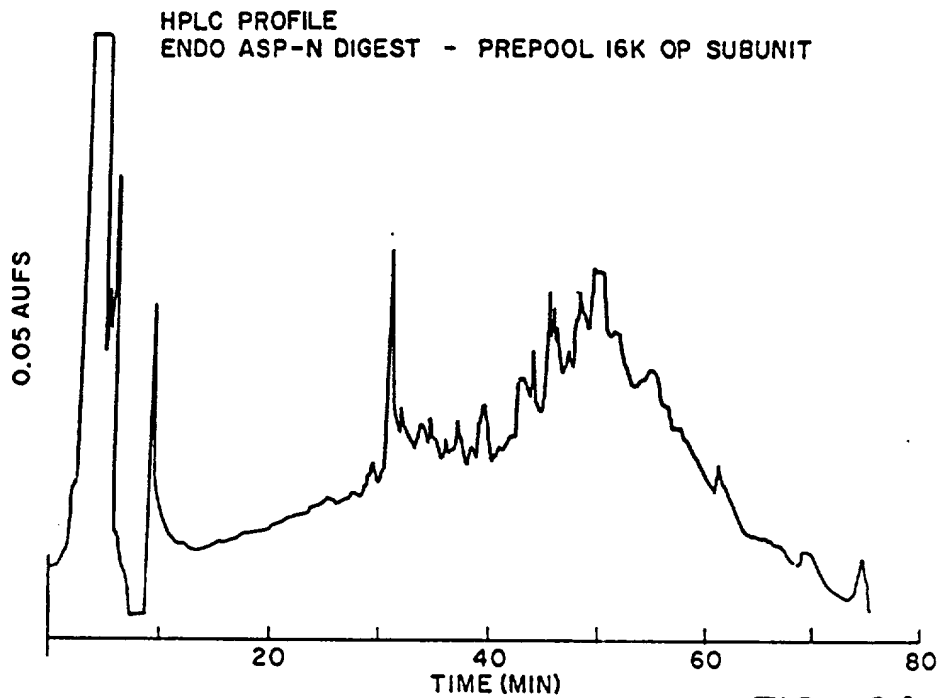


FIG. 16A

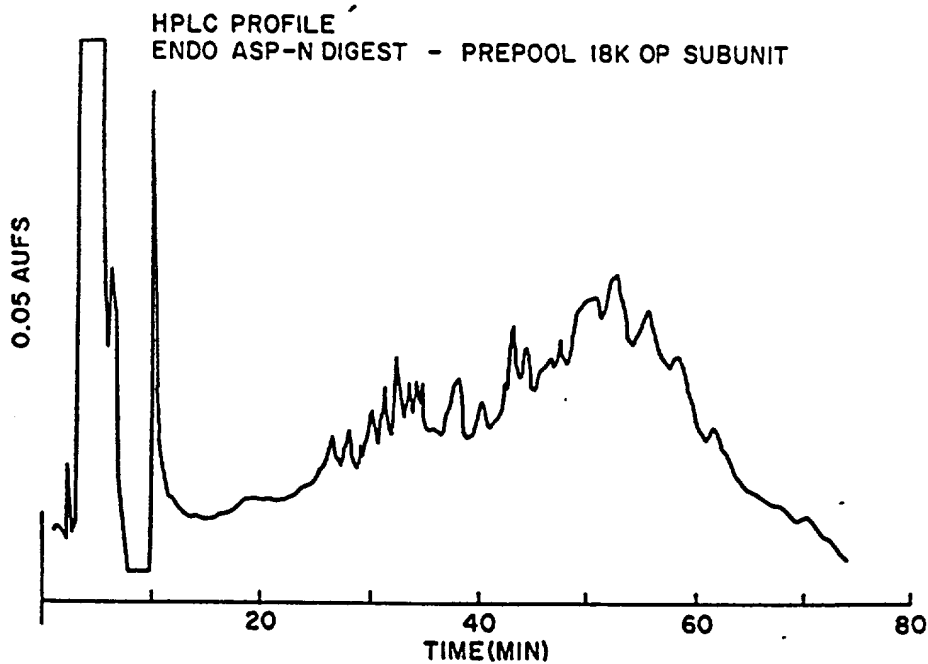


FIG. 16B

Microscopic

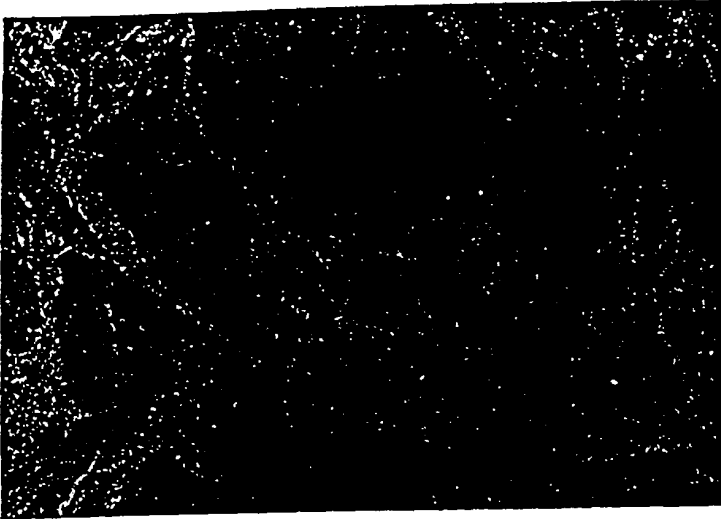


FIG. 17A

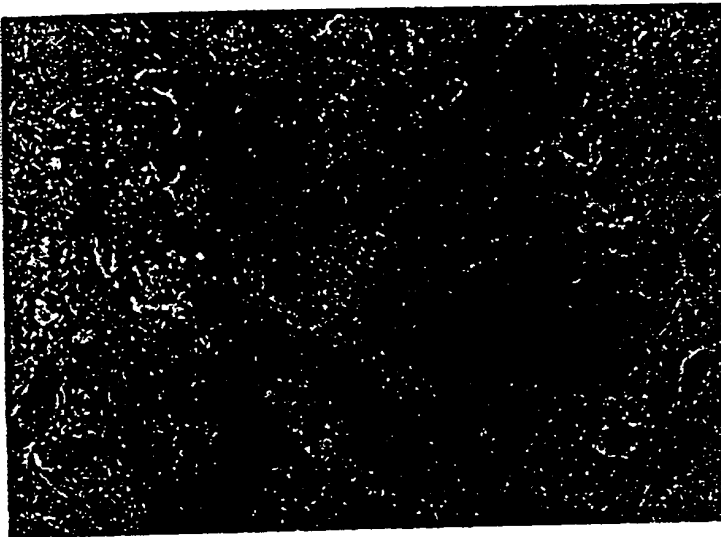


FIG. 17 B

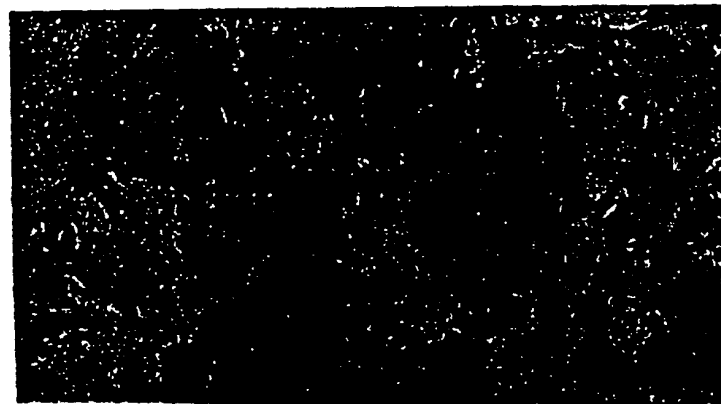


FIG. 17C

[illegible]

FIG. 18-1

FIG. 18-2

FIG. 18-3

FIG. 18-4

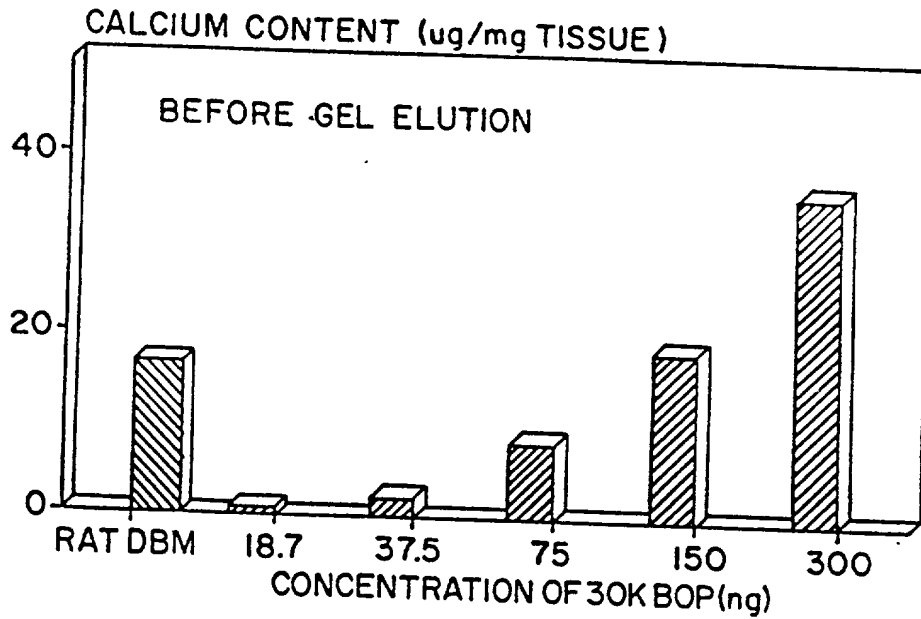


FIG. 20A

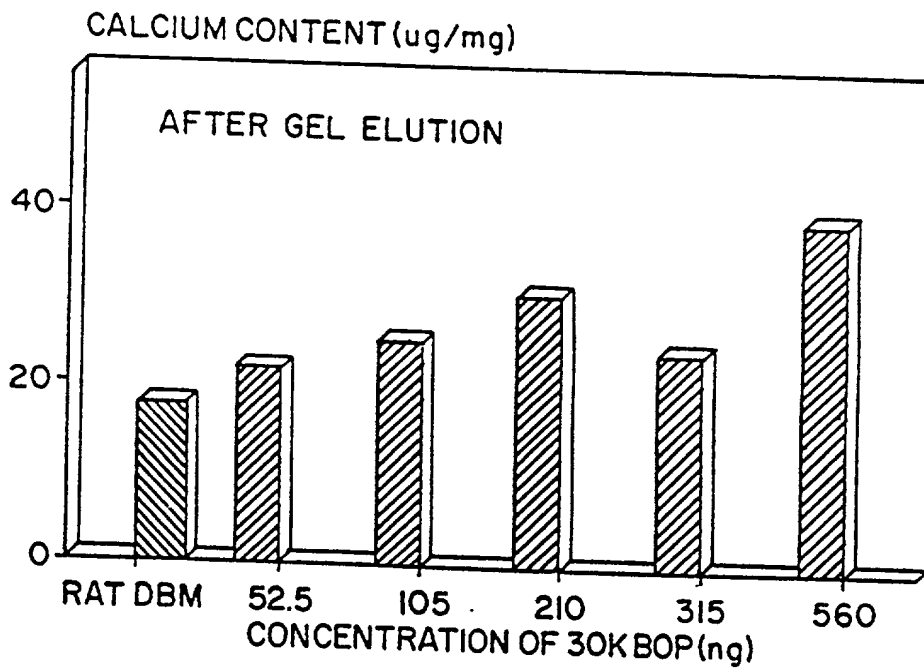


FIG. 20B

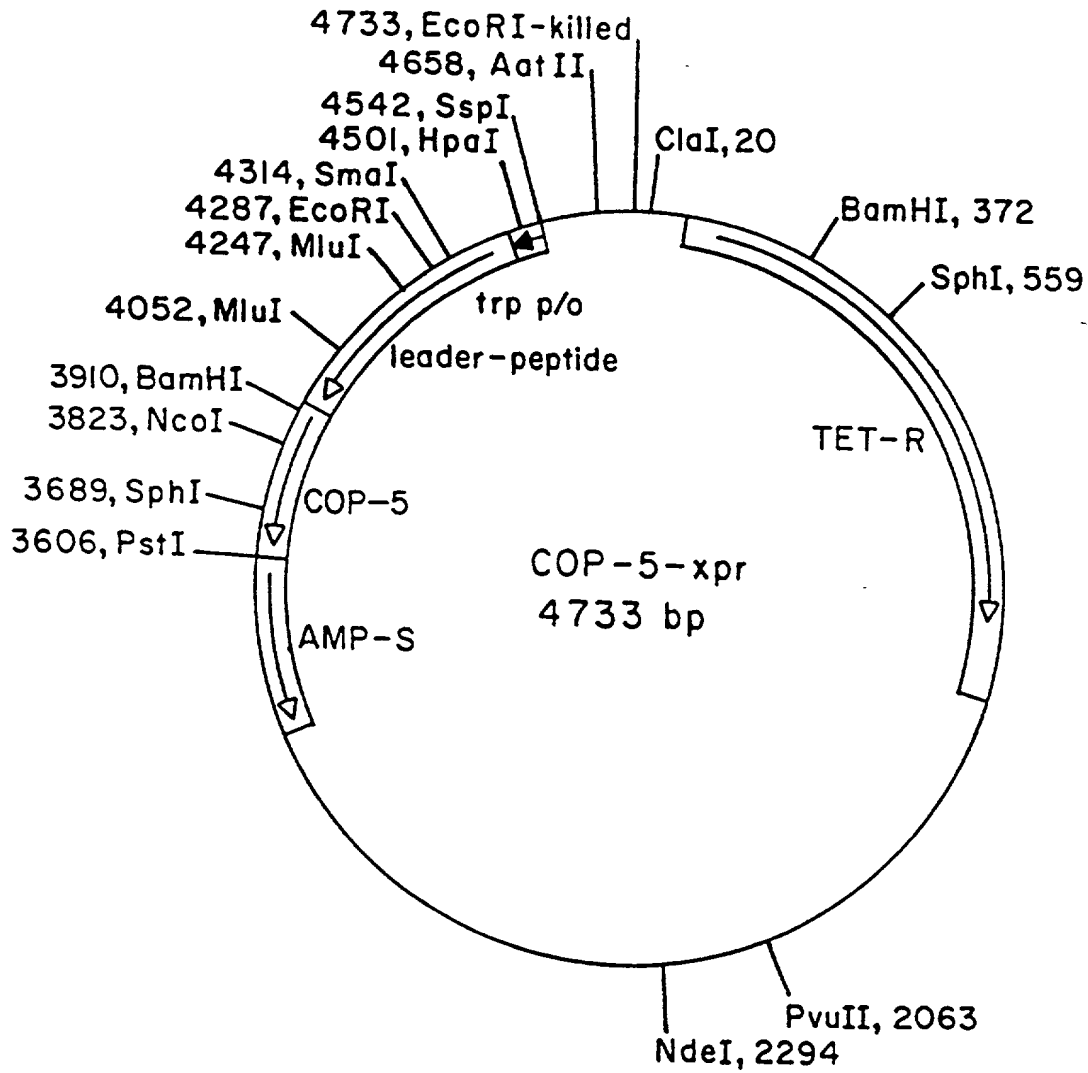


FIG. 21A

COP-5 fusion protein

10 20 30 40 50
ATGAAAGCAATTTTCGTACTGAAAGGTTCACTGGACAGAGATCTGGACTC
M K A I F V L K G S L D R D L D S
BglIII

60 70 80 90 100
TCGTCTGGATCTGGACGTTTCGTACCGACCACAAAGACCTGTCTGATCACC
R L D L D V R T D H K D L S D H

110 120 130 140 150
TGGTTCTGGTCGACCTGGCTCGTAACGACCTGGCTCGTATCGTTACTCCC
L V L V D L A R N D L A R I V T P
Sall Sma

160 170 180 190 200
GGGTCTCGTTACGTTGCGGATCTGGAATTCATGGCTGACAACAAATTCAA
G S R Y V A D L E F M A D N K F N
I EcoRI

210 220 230 240 250
CAAGGAACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGA
K E Q Q N A F Y E I L H L P N L
MluI BglIII BspMI+

260 270 280 290 300
ACGAAGAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCT
N E E Q R N G F I Q S L K D E P S
HindIII

310 320 330 340 350
CAGTCTGCGAATCTGCTAGCGGATGCCAAGAACTGAACGATGCGCAGGC
Q S A N L L A D A K K L N D A Q A
NheI FspI

360 370 380 390 400
ACCGAAATCGGATCAGGGGCAATTCATGGCTGACAACAAATTCAACAAGG
P K S D Q G Q F M A D N K F N K

410 420 430 440 450
AACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGAACGAA
E Q Q N A F Y E I L H L P N L N E
MluI BglIII BspMI+

460 470 480 490 500
GAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCTCAGTC
E Q R N G F I Q S L K D E P S Q S
HindIII

FIG. 21B-1

510 520 530 540 550
TGCGAATCTGCTAGCGGATGCCAAGAACTGAACGATGCGCAGGCACCGA
A N L L A D A K K L N D A Q A P
NheI FspI

560 570 580 590 600
AGGATCCTAATGGGCTGTACGTCGACTTCAGCGACGTGGGCTGGGACGAC
K D P N G L Y V D F S D V G W D D
BamHI SalI

610 620 630 640 650
TGGATTGTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGCGAATG
W I V A P P G Y Q A F Y C H G E C
StuI NcoI BsmI+

660 670 680 690 700
CCCTTTCCCGCTAGCGGATCACTTCAACAGCACCAACCACGCCGTGGTGC
P F P L A D H F N S T N H A V V
NheI DraIII
PflMI

710 720 730 740 750
AGACCCTGGTGAACCTCTGTCAACTCCAAGATCCCTAAGGCTTGCTGCGTG
Q T L V N S V N S K I P K A C C V
MstII

760 770 780 790 800
CCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATGAGAA
P T E L S A I S M L Y L D E N E K
SphI

810 820 830 840 850
GGTGGTGCTGAAGAACTACCAGGAGATGGTAGTAGAGGGCTGCGGCTGCC
V V L K N Y Q E M V V E G C G C
PflMI

860
GCTAACTGCAG
R *
PstI

FIG. 21B-2

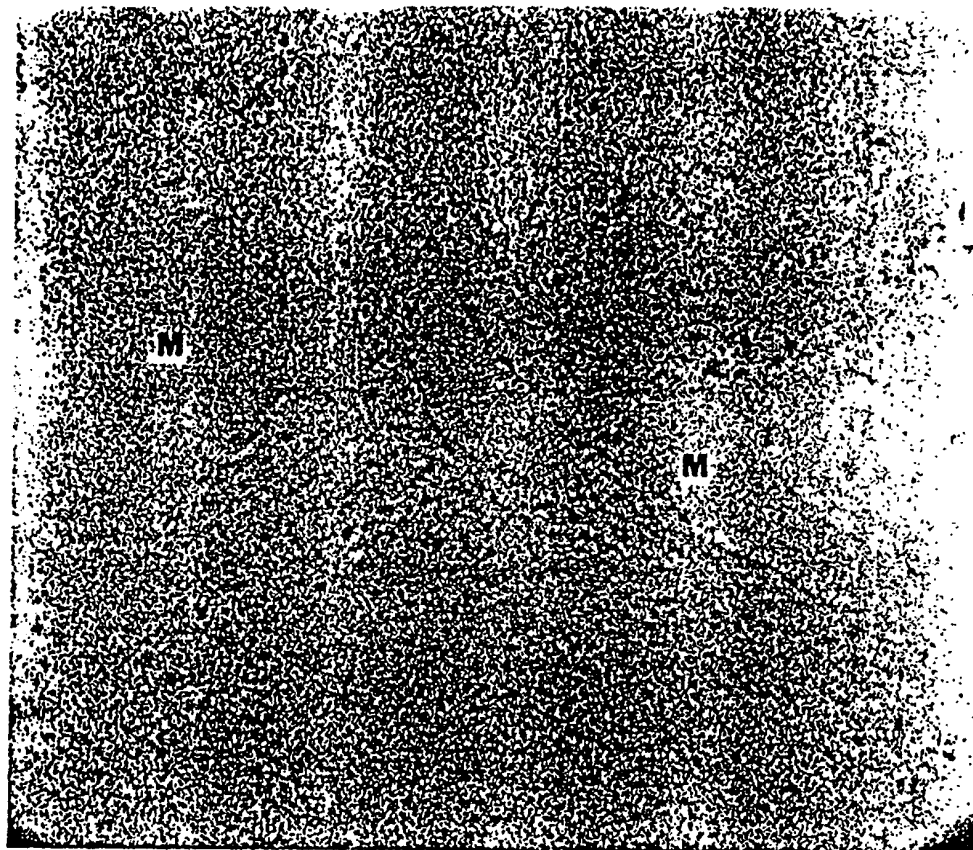


FIG. 22A

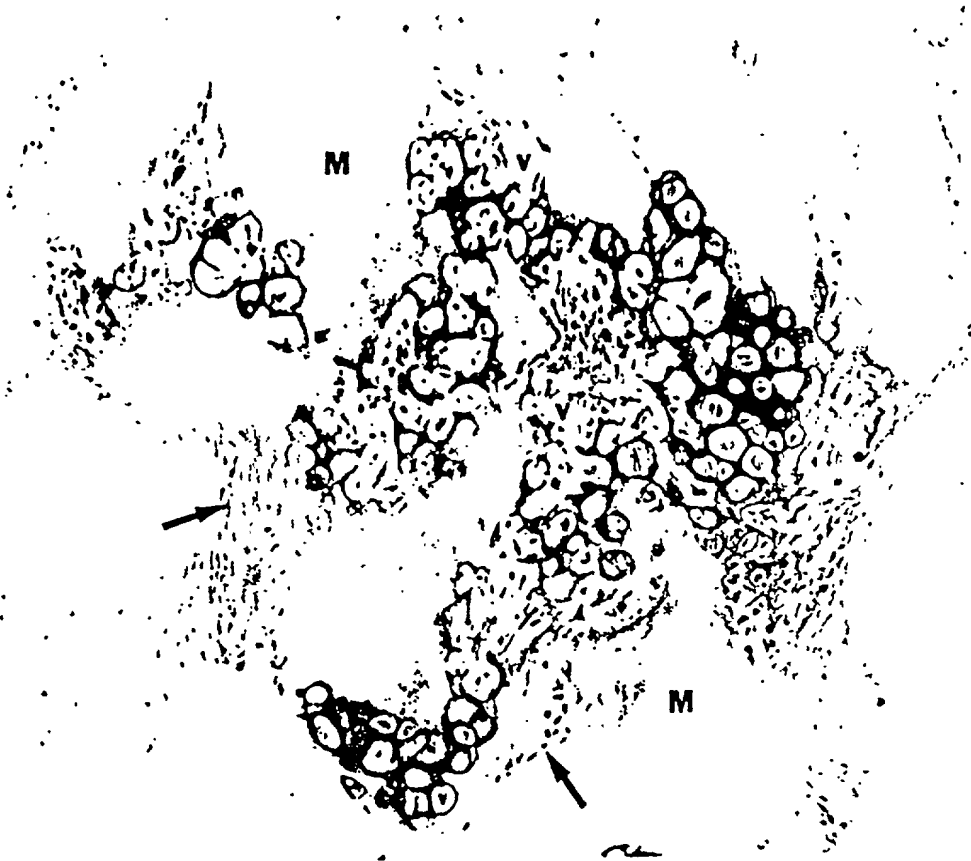


FIG. 22B